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ENVIRONMENT AND STRYCHNINE SULPHATE: EFFECTS
ON MAZE BEHAVIOR OF THE RAT

BY



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The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled Environment and Strychnine Sulphate: Effects on Maze Behavior of the Rat submitted by Norman Eugene Shandro in partial fulfilment of the requirements for the degree of Master of Science.

ABSTRACT

The effects of two levels of each of three factors were assessed by the performance of rats in a Hebb-Williams maze. The factors were: (1) enriched or restricted rearing environments, (2) strychnine or saline injections during rearing, and (3) strychnine or saline injections during maze training. A total of 64 male, albino, Wistar rats, in litters of 8, were run in two replications. The injections of either .16 mg/kg strychnine sulphate or isotonic saline were administered once a day from ages 40 to 51 days during the Ss' experience of the rearing environments. Injections were also administered immediately after the first trial of each of the twelve problems in the Hebb-Williams maze which encompassed days 70 to 81 of the Ss' lives. The Ss were run eight trials on each of the problems in the following manner. On the first day Ss were given one trial on Problem I then immediately injected. Twenty hours later Ss were run for seven more trials on Problem I and four hours later they received the first trial on Problem II and were injected. This procedure continued throughout the twelve problems. It was assumed that the performance on trial 2 would provide a measure of consolidation and that the performance on trials 3-8 would provide a measure of problem solving ability.

The general findings were that strychnine significantly disrupted consolidation in those Ss raised in a restricted environment but enhanced consolidation of Ss raised in the enriched environment. With respect to problem solving ability, it was found that Ss reared in an enriched environment were superior to those reared under restricted conditions; in addition while strychnine significantly improved this ability in the enriched groups, it had no effect in the restricted groups. The results were discussed in relation to possible differential capacities for consolidation in the differently raised rats.

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INTRODUCTION

In recent years there has been an increasing interest in the study of the effects of two different kinds of variables upon learning ability. These variables are:

(1) the administration of drugs, and (2) the modification of the animal's environment during rearing. While individually each of these variables has generated a great deal of research, they have never been studied concurrently. This study was undertaken to determine the combined effects of rearing environment and a drug. Specifically, sub-convulsive doses of strychnine sulphate.

The Drug. The action of strychnine sulphate (hereinafter referred to as strychnine) in the central nervous system (CNS) and particularly in the spinal cord is quite well known. It acts as a powerful stimulant indirectly by blocking post-synaptic inhibition (Andersen, Eccles, Løyning, & Voorhoeve, 1963). In the spinal cord the excitation occurs through the blocking of the action of post-synaptic inhibitory synapses which are formed by a variety of converging motoneurones (Bradley, Easton, & Eccles, 1953; Curtis, 1959; Curtis, 1962; Eccles, Fatt, & Koketsu, 1954).

At higher levels of the CNS this inhibition due to strychnine has been found in the sensory fiber terminals of

the olivo-cochlear bundle and in the hair cells of the organ of Corti (Desmedt & Monaco, 1960). In addition, excitation is shown in the electrocorticogram after local application to the cerebral cortex (Purpura & Grundfest, 1957) and in the electroencephalogram after systemic administration of strychnine (Heinbecker & Bartley, 1939). Andersen et al. (1963) report that pyramidal cells of the hippocampus, Purkinje cells in the cerebellum, and the relay cells of the ventrobasal complex are all resistant to the effects of strychnine. They suggest that perhaps these cells do not have the same transmitter substance as those responsible for inhibition in the spinal cord, or that the transmitter substance may be the same but the receptor sites of the synaptic membrane may differ between various parts of the nervous system. In this second case, strychnine may differ in its effect on account of the effectiveness of its competitive attachment to the receptor sites of the inhibitory synapse on various cells.

Drug-learning Experiments. The enhancement of performance by strychnine in a maze was first reported by Lashley (1917). He found that low doses of strychnine facilitated performance of rats in a Watson maze. However, the replication failed to support this finding. This may have been due to the fact that, in the replication, older and heavier animals were used while the same dosage of the drug was used on all animals. The dose that had proved effective in the lighter group may have been insufficient

to produce facilitation in the heavier group used in the replication.

This observation was ignored for several decades until McGaugh and Petrinovich (1959) decided to test the finding while applying a control for the weight of their subjects. They found that while the three drug groups (1.00, 0.66, and 0.33 mg./kg. body weight) did not differ among themselves, the experimental subjects made fewer errors in a Lashley III maze than did the pooled control groups.

Since 1959 a number of studies have shown a facilitating effect of strychnine on several problems, including maze learning (Cooper & Krass, 1963; Greenough & McGaugh, 1965; McGaugh, 1961; McGaugh, 1967; McGaugh, Thomson, Westbrook, Hudspeth, 1962; Petrinovich, 1967; Ross, 1964), escape and avoidance learning (Bovet, McGaugh, & Oliverio, 1966; Gibby, Gibby, Kish, & Theologus, 1965; Keleman & Bovet, 1961), discrimination learning (Calhoun, 1966; Krivanek & Hunt, 1967; McGaugh & Thomson, 1962; Petrinovich, 1963), delayed alternation (Petrinovich, Bradford, & McGaugh, 1965), oddity (Hudspeth, 1964), latent learning (Westbrook & McGaugh, 1964), and classical conditioning (Benevento & Kandel, 1967). It is obvious then, that facilitation has been obtained across many situations.

In many of these studies subjects were given the drug a few minutes before the training sessions. As a result the animals were trained while under the drug's influence. Using

this procedure it is difficult to discover the basis of the drug's effect on the animals' behavior. The improvement shown may have been due to the action of the drug on consolidation, learning, or performance, or some combination of the three. McGaugh and his coworkers feel that the enhancement shown comes about as a result of improved consolidation; that is, because of the excitatory action of the drug, the neural traces of an experience persevere for a longer period and, as a result, are more likely to enter a more permanent memory storage. This would lead to better learning since the animal would require less experience in a situation in order to retain some relatively permanent trace of the experience which would, in later trials, lead to better performance. Since learning can only be measured by some sort of performance on a task and superior learning is inferred from better scores on some dependent variable, it is important that if one is to infer superior learning there is no confounding of effects which would be transiently affecting performance. In the case of pretrial drug injections such a confound may occur since the improved scores of the drug groups may be due to a transient change in motivation, attention or motor activity. For example, Benevento and Kandel (1967) classically conditioned cats for forepaw flexion to a train of clicks. In those subjects under the influence of strychnine, conditioned responses were more frequent than in those under saline, and the proportion of conditioned

responses increased with numbers of reinforced trials only in the strychnine group. The authors suggested that this enhancement may have been due to the reduction of behavioral inhibition, analogous to Hull's (1951) reactive inhibition. The net effect of such a reduction of inhibition would be an increased drive while under the influence of the drug.

In opposition to the view held by McGaugh and his coworkers, Thiessen, Schlessinger, and Calhoun (1961) suggested that:

"A drug whose effects begin after a learning trial could result in better learning for at least three reasons: (a) it could further stimulate the action of relevant stimulus cues, as hypothesized by McGaugh and Petrinovich; (b) it could hamper the functioning of sensory mechanisms thus cutting down on the amount of interfering stimuli reaching the brain; or (c) it could alter the response of the animal to reduce potentially interfering stimuli reaching the brain."
(p. 493)

In their study with two strains of mice, Thiessen et al. chose to focus on the latter two possibilities. Locomotor activity immediately after an intraperitoneal (IP) injection of either 1.00 mg/kg strychnine or saline was measured. In addition to strain differences, they found differences between drug and control groups with the strychnine animals showing less locomotor activity as measured by square crossings in an open field. This finding suggested that strychnine has a possible depressing effect on motor behavior and it was argued that "... the learning effects attributed to central nervous system stimulation can be explained by decreased post-trial interference."

(p. 496), since fewer stimuli would be impinging on animals with reduced motor activity.

McGaugh and Petrinovich (1963) replied to the above cited study by presenting a criticism of both the procedure and the interpretation involved in the work of Thiessen et al. The criticism of the procedure pointed out that the situation used had no direct bearing on the question of the learning effects of strychnine. The animals were satiated on food and water and placed in a novel situation; a single dose of drug was used; this dose was quite high for the species used (mice); and there was no evidence that such a dose would have facilitated learning.

Furthermore, McGaugh and Petrinovich pointed out that an interpretation based on decreased post-trial interference was valid only where one trial a day was used, since if there was more than one trial, the succeeding trials and the handling between trials would constitute post-trial interference. In several studies massed trials were used (McGaugh & Petrinovich, 1959; McGaugh & Thomson; 1963; McGaugh, Thomson, Westbrook, & Hudspeth, 1962) and the explanation could not hold in these cases. It could hold, however, for post-trial injection situations since immediately after the trial and injection the animal is usually placed in a situation (his home cage or some quiet holding cage) where stimulation and resulting interference are greatly reduced. Thiessen et al., however, refer to decreased

locomotor activity with strychnine, and this fact is not well-established since there is evidence that locomotor activity is increased by low doses of strychnine and decreased by high doses (Dews, 1953). Theissen et al. may have used one of the high doses that decreases this activity.

In another study of locomotor activity after strychnine injections Carlson (1964) tested rats in an observation box. Injections of 0.10, 0.30, and 0.70 mg/kg produced no difference from the control group on exploration as measured by walking, rearing, and sniffing. If one accepts these measures of exploration as equivalent to locomotor activity, this study contradicted Thiessen et al. The contradiction is even stronger against the interpretation of Thiessen et al. since these are the doses that have sometimes been found to facilitate learning in rats.

To accept the notion that enhanced performance in a learning situation comes about as a result of improved memory storage through improved consolidation (or improved learning) due to the stimulation of the CNS as suggested by McGaugh (1967), there must be evidence in addition to that provided by experiments where animals are trained and tested while drugged. As stated, under the drugged condition, learning itself may not be affected but performance may be enhanced by transitory effects of the drug that are present in the training and testing situations but that do not have long term effects. Such

additional evidence may be provided by experiments that utilize post-trial injections of the drug, since in this case both groups (experimental and control) are in the training situation under the same conditions and any effects of the injection are felt under conditions different from those of the learning situation.

There are several studies in the literature that have used post-trail injections. The first was that of McGaugh, Thomson, Westbrook, and Hudspeth (1962) which measured learning in the Lashley III maze by male and female Tryon S_1 (maze bright) and S_3 (maze dull) rats. They used an injection of 1.00 mg/kg strychnine either 6 min before (B-6) or 1 min, 15 min, 30 min, or 90 min after (A-1, A-15, A-30, A-90) a daily maze trial. On the basis of the number of errors made on trails 2-8 groups A-1 and A-15 did better than groups A-90 and B-6, and group A-15 was superior to A-30. Strain and sex differences were also found. Due to the interaction of both strain and sex, the effect of the drug was not clear. In addition there was no non-strychnine control group.

In 1964 Hudspeth trained male Long-Evans hooded rats on an oddity problem preceded by a discrimination and discrimination reversal problem. They were injected with either 0.20 mg/kg strychnine or saline 30 sec. after the final trail of a daily block of 12 trails on the oddity problem. The drug group performed significantly above chance while the control group

responded at a chance level.

In an incomplete study, Ross (1964) reported on the performance of S_1 and S_3 rats in a 14 unit alley maze. They were given one trial a day and injected with either strychnine (concentration unreported) or saline 1 min or 1 hr after the trial. The facilitation was found (no data reported), but the S_3 rats were superior to the S_1 's at the one minute interval and were not affected at the one hour interval while the S_1 's showed improvement at both intervals. Here again there was the confounding effect of strain.

Greenough and McGaugh (1965) employed male and female rats of the Sprague-Dawley strain in testing the effects of strychnine on the learning of a Lashley III maze. Their SB group received 1.00 mg/kg of strychnine before 2 training trials in the maze and saline immediately after these 2 trials. The C group received saline immediately after the training trials and 48 hrs before the 5 retention trials which occurred 6 days after training. Group SI was injected with strychnine immediately after the training trails and with saline 48 hrs before the retention trials. Group SD received saline immediately after training and strychnine 48 hrs before retention. If strychnine affected performance, then SD should have made the fewest errors, and if it affected consolidation, group SI would be the best. There were no significant differences between the groups on the training trails, but by using only the first

3 of the 5 retention trials, SI females were found to be superior to C and SD females. The combined sex scores of the SI group were better than those of the SD group. Here it was necessary to make a post hoc selection of a part of the data (3 of 5 retention trials) to obtain significant differences. Also this effect was not the same for both sexes.

Immediate post-trial injections of strychnine (0.15, 0.30, and 0.60 mg/kg) were administered to DBA/2J mice by Bovet, McGaugh, and Oliverio (1966). Enhanced avoidance in a shuttle box was found with the 0.15 and 0.30 doses but the 0.60 dose and an injection of 0.30 delayed for 1 hr after the trials proved ineffective. The greatest effect was shown on the second of 5 daily training sessions of 100 trials each.

In a rather complex study Calhoun studied mice of the C57BL/Cr1g strain in a two choice spatial discrimination task. After a daily block of 10 trials the subjects were injected with either 0.60 mg/kg of strychnine or saline. He found a facilitative effect of strychnine but only when his additional variable of disrupting stimulation was low.

The most recently reported study in which post-trial injection of strychnine was used is that of Krivanek and Hunt (1967). Male Wistar rats received three massed trials daily on a black-white discrimination problem. Immediately after the third problem the subjects were administered injections of either 0.33 mg/kg strychnine or saline. The strychnine group

proved to be superior to the saline group on total errors during learning.

As can be seen from the description of the foregoing studies there are many factors that enter into the determination of a specific facilitative dose of strychnine. Differences can arise due to strain, species, sex, task, extraneous stimulation, and time of injection. McGaugh (1967) who holds that strychnine is indeed a general facilitator of learning, suggests that such factors as these may be responsible for the inconsistent or no effect experiments reported.

The earliest reported no effect study was that of Prien, Wayner, and Kahan in 1963. Blinded female hooded rats and doses of 1.00, and 0.75 mg/kg strychnine were employed in an elevated T maze task. The injections were administered 20 min before the daily trial. They found no effect of the strychnine injections. Petrinovich (1967), however, used hooded rats and found that only a dosage of 0.125 mg/kg showed facilitation over the control group as measured by errors in a Lashley III maze. Dosages of 0.25, 0.50, 1.00, and 1.50 did not differ from the control. Animals that received a dose of 1.75 mg/kg actually exhibited significantly poorer performance than the controls. This would suggest then that the findings of Prien et al. may have been the result of using an excessively large dose of the drug for the strain of rat employed.

Loutitt (1965), using female hooded rats and a dose of 1.00

mg/kg in a Lashley III maze found a significant improvement in trials to criterion but no difference in total errors to criterion. The same argument as above might apply here since the dose may have been too high to show the facilitation on the error measure.

Doolittle and Thomson (1966) trained S_1 and S_3 rats (males and females) one trial a day for 10 days in a 6-unit multiple-U maze. Thirty sec after reaching the goal, strychnine was applied topically via an implanted cannula. The strychnine group did not differ from the saline controls. The lack of facilitation may be attributed to the concentration used or to the fact that strychnine is considered more a spinal than a cortical stimulant (Purpura & Grundfest, 1957). There is, however, evidence that topical application of the drug brings about changes in the electrocorticogram (Purpura & Grundfest, 1957) indicating some cortical effect.

Otis and Prior (1968) trained female rats of the S_1 and S_3 strains in a Lashley III water maze with 20 trials being delivered over 5 days. The subjects were injected with 1.00 mg/kg strychnine or saline immediately after the last trial of the day. No facilitation by strychnine was found. In addition, using Long-Evans hooded rats in the same maze, no drug facilitation was present with doses of 0.10, 0.20, 0.40, and 0.80 mg/kg. In this case the lack of positive findings may have been due to the nature of the task. It seems that a water maze is

quite different than a Lashley III maze used with food reward.

The report of Schaeffer (1968) used male Sprague-Dawley rats in a Lashley III maze for food reward. In the three reported experiments doses of 0.08, 0.16, 0.32, 0.64, and 0.33 mg/kg demonstrated no improved performance as measured cul errors, total errors, or speed scores.

Even if all of the no effect experiments can be explained in terms of parameter differences, there remains one problem for the interpretation that strychnine facilitates learning rather than performance, and that is the study of Cooper and Krass (1963). They trained female hooded rats to run for food and to avoid foot-shock in a Hebb-Williams maze. They were trained on practice problems (Rabinovitch & Rosvald, 1951) for 2 weeks and on the day prior to injection they were run to a criterion of 5 out of 6 trials in 10 sec or less. The next day they were injected with 1.25/mg/kg strychnine or merely given the needle. Half of each of the above groups were trained on problem 2 of the series of test problems 24 hr later and half were trained 72 hr later. At both intervals the subjects that received strychnine made fewer errors than their controls. This implies that the effects of strychnine may not be as short-lived as believed. Goodman and Gilman (1965) report that doses of strychnine taken orally are being excreted in the urine within minutes after being administered and that

excretion is virtually complete after 10 hr although traces may be found several days later. This data is reported for humans, however, and species differences are probably present. Also, the remaining traces or some unknown post-drug effect may have some behavioral influence. In the light of these considerations it is possible that daily post-trial injections may involve some trace pre-trial effects.

It appears that, ideally, to show that strychnine shows its effects by influencing learning one must use a situation where a retention trial occurs some time after a single training session which had been followed by a single injection of the drug.

While some experimenters interpret the data in the light of strychnine's CNS effects, and therefore effects on a postulated learning process in the CNS, there are other possible interpretations. The drug may produce its effect by rather immediate and transitory effects on drive, arousal, or motor activity and thereby influence performance rather than learning. However, the usefulness of the drug in producing better maze behavior is not dependent on one's theoretical view as to how the improvement comes about. It is worthwhile to continue the investigation of the drug effects themselves. It would be of interest, if it were present, to discover an interaction between this drug and other factors which have been shown to affect learned behavior (e.g., rearing in an enriched

environment). Furthermore, since the drug might have long-lasting effects, it could be used during the rearing period to determine if these possible effects can modify those of the rearing environment.

Enriched Environment Experiments. Work on the second factor of enriched rearing environments was initiated by Hebb (1949). He compared the learning ability of rats reared in small cages with that of rats who were raised as pets in a home and found that the second group learned a Hebb-Williams test more rapidly. Forgays and Forgays (1952) extended this experiment with additional controls. They used a 4 layer cage to provide different experimental environments within the same general environment. There were 7 different groups ranging from free environmental (FE) with access to various playthings to restricted (R) who were housed singly in small metal cages with limited opportunity for visual stimulation. Other groups were housed in round wire mesh cages within the FE condition. The subjects remained in a particular environment from 26 to 90 days of age at which time all were placed in colony cages and pretraining was begun in the Hebb-Williams test. The overall finding was that FE animals showed superior performance on the test than restricted animals on the measure of errors and that the degree of enrichment was significant (FE animals with playthings made significantly fewer errors than FE animals who had no playthings.).

These results were confirmed by Hymovitch (1952) with some additional findings, in one experiment he used free environment (G1); mesh cages that allowed little free movement but offered free vision (G2); enclosed activity wheels which allowed motor activity but restricted visual experience (G3); and circular metal "stovepipe" cages that restricted both locomotor and visual activity (G4). Groups 1 and 2 were superior to groups 3 and 4 and there was no difference between G1 and G2 or between G3 and G4. Another experiment in this same report moved FE animals to stovepipe cages and stovepipe animals to FE cages. Before the change, subjects had spent the period from 35 to 75 days of age in the first environment and after the change they were maintained in the altered conditions for 45 days after which they were tested. The group that had received free environmental experience early in life were superior to those who received it later.

From this we may conclude that: (1) free environment early in life gives rise to superior ability in learning later; (2) motor factors are of little importance while visual factors may have a large effect; (3) the enriched experience must take place early in life; (4) the effects are relatively permanent.

Bingham and Griffiths (1952) compared enriched environment (G1), restricted locomotor but free visual environment (G2), and the normal laboratory rearing situation (G3). The first

two groups were in the experimental situation from 21 to 51 days of age at which time they were placed in laboratory cages. All animals were tested at 82 days of age in an inclined plane maze. G2 and G3 showed no differences so were summed together for comparison with G1. It was found that G1 was superior to the combined groups. This confirms again the conclusion that enriched early experience improves learning ability but does not confirm that visual experience plays an important role.

A study that supports the general finding that animals from enriched environments exhibit superior learning but puts forth a different theoretical point of view is supplied by Woods, Fiske, and Ruckelschaus (1960). In this experiment the rearing cages were similar to those described in Forgays and Forgays (1952) as was the procedure except that there was the added factor of drive intensity. The low drive groups were run 24 hrs hungry in a Hebb-Williams maze. The high drive groups had the additional incentive of shock avoidance. Under low drive the expected results occur (i.e., enriched superior to restricted) however there is no difference in the high drive groups. From this, Woods et al. state that, "The improvement produced in the restricted animals led to the conclusion that their characteristically poor problem-solving performance is not due to a deficiency in intelligence or maze solving ability, but more likely due to a heightened exploratory

drive." (p. 169)

In the previous studies there is no claim, however, that restricted animals are necessarily deficient in problem-solving ability. From Bingham and Griffiths (1952) one might conclude, in fact, that they are equivalent to those raised in a normal laboratory environment. The suggestion is rather, that the enriched environment brings about superior ability and in the case of Woods, Fiske, and Ruckelschaus the high drive restricted group may simply be elevated to perform at an asymptote which the enriched group is able to achieve irrespective of drive level.

The idea of differential learning ability arising from varied environments during rearing was extended by Krech and his colleagues (Diamond, Krech & Rosenzweig, 1964; Krech, Rosenzweig, & Bennett, 1960, 1962; Rosenzweig, 1966; Rosenzweig, Krech, Bennett, & Diamond, 1962). In addition to studying the behavioral results of early enriched environments, they have studied its effects upon the morphology and biochemistry of the brain. The basic procedure in these studies is to use 2 groups Rosenzweig (1966). In the environmental complexity and training group (ECT) subjects are raised 10-12 in a large cage from weaning onwards. In the cage were toys such as ladders, wheels, and platforms. These animals, in groups of 5 to 6, are allowed daily half-hour exploratory sessions in an open field with movable barriers which are changed daily.

After about 30 days they receive some formal maze training. Food and water is supplied ad lib in the home cages. Under the impoverished condition (IC), the animals are raised in small individual cages with solid walls so they cannot see their neighbours. The cages are kept in a quiet, dimly lit room and food and water are supplied ad lib.

Behaviorally, Krech, Rosenzweig, and Bennett (1962) showed that ECT animals are superior to IC animals in learning of the Krech Hypothesis Apparatus--which is essentially 4 successive units of 2-choice discrimination boxes. A discrimination-reversal technique was used. The results show that the groups are equivalent on the original discrimination but they begin to grow apart during succeeding days of reversal. If the inferior performance of the IC group were due to a "heightened exploratory drive" as suggested by Woods et al. (1961), this group should be inferior on the original discrimination as well.

The Problem. It has been shown that the injection of strychnine seems to improve learning ability in rats. Further, it has been shown that early experience in an enriched environment seems also to lead to superior learning ability. Therefore, this experiment was undertaken to determine the combined effects of these two variables. As there is some indication that the drug may have a lasting behavioral effect (Cooper & Krass, 1963), it was administered not only during a

learning experience, but also during the early experience of an enriched or restricted environment. Because of the possibility of complex interactions of these factors and the lack of pertinent data, no interaction predictions were made. It was predicted, however, that there would be a main effect of rearing environment (enriched superior to restricted) and that there would be a main effect of the injections at the time of testing (strychnine superior to saline).

METHOD

Subjects

The Ss were 64 male albino rats of the Wistar strain obtained from Woodlyn Farms of Guelph, Ontario. They were 21 days old at the beginning of the experiment, and 8 litters of 8 each were used.

In the first replication, one S in group RCS (see below) was ill from the eighth day of testing onward and died the day after testing was completed. However the data from this animal proved to be equivalent to that of others in that group so it was retained. The average weight of the Ss at the beginning of the experiment was 73 gms.

Design

The design was basically a 2 x 2 x 2 factorial. The factors were: (1) rearing environment, (2) type of injection during rearing, and (3) type of injection during testing. From these treatments arose the 8 experimental groups, which were designated:

EDD - enriched environment, drug early, drug during testing

EDC - enriched environment, drug early, saline during testing

ECD - enriched environment, saline early, drug during

testing

ECC - enriched environment, saline early, saline during
testing

RDD - restricted environment, drug early, drug during
testing

RDC - restricted environment, drug early, saline
during testing

RCD - restricted environment, saline early, drug during
testing

RCC - restricted environment, saline early, saline
during testing

Two additional factors arose in the design. The study was run with a replication due to the time required to process the Ss, so replications became a factor. Littermates were used as a control factor and 4 litters were used in each of the original and the replication. Each litter supplied one S to each of the above groups.

Apparatus

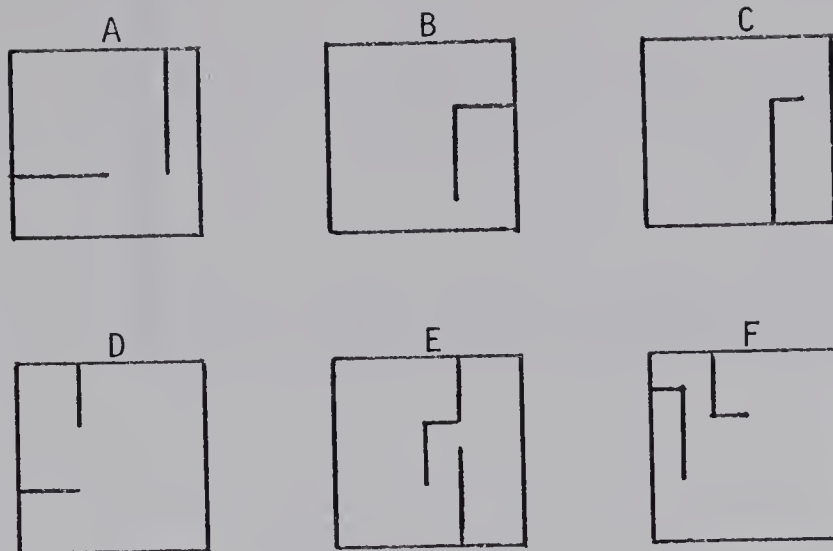
Rearing Cages. One half of the Ss in each replication were housed in group cages, 8 per cage. These cages were designed after Krech, Rosenzweig, and Bennett (1960). The overall dimensions were 24 in x 30 in x 18 in high. Two opposite sides were of unpainted plywood and the back, front, top, and bottom were a wooden framework covered with hardware cloth.

At the back of the cage was a 4 in wide wooden platform mounted 10 in above the floor. A hardware cloth ramp led from the front of the cage up to the center of this platform. Mounted in the cage was a plastic ladder, a plastic parakeet ferris wheel, a wooden ramp 2 in wide, 3 1/2 in high, and 10 in long, a square wooden "tunnel" was supplied to allow some shelter from the light during the day part of the diurnal cycle. Two marbles, a bell, and a small, opaque glass bowl were lying free in the cage.

The remainder of the Ss were housed in the restricted condition. They were housed singly in metal cages with only the front being made out of mesh and the rack of cages was turned to a wall in a room separate from the colony room so as to minimize visual and auditory stimulation.

The Maze. A Hebb-Williams closed field maze as described by Rabinovitch and Rosvald (1951) was used. It consisted of a box 30 in x 30 in x 5 in high with a wire mesh lid. There were a series of movable barriers interposed between the start and goal boxes located at diagonally opposite corners. The floor was grooved at 5 in intervals to support the barriers and to mark out the error zones (Fig. 1). The walls and the floor were painted flat gray. A modification suggested by Schiller and Chorover (1966) was used in that the start alley consisted of an L-shaped alley (Fig. 2) which enabled the experimenter to remain in one position to

Practice Problems



Test Problems

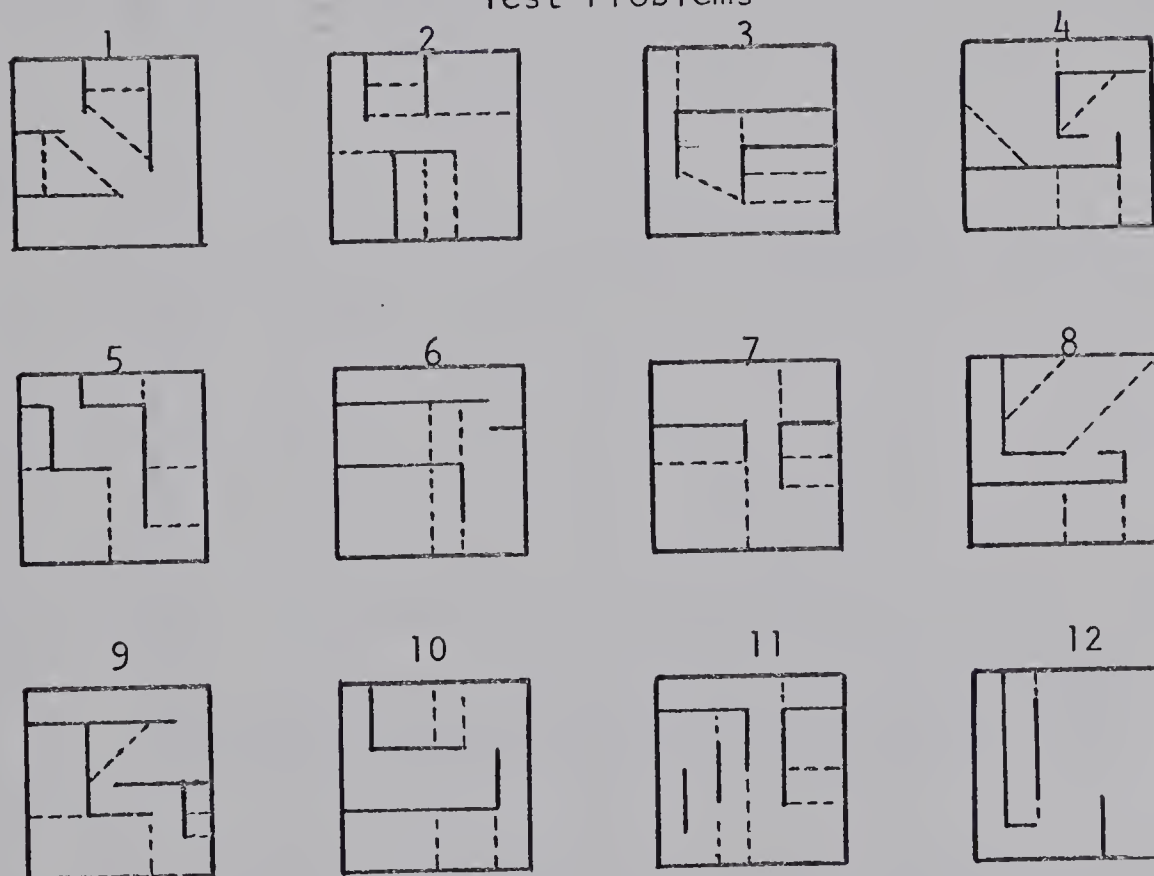


Figure 1. Floor Plan of the Training and Test Problems Showing the Error Zones (Broken Lines)

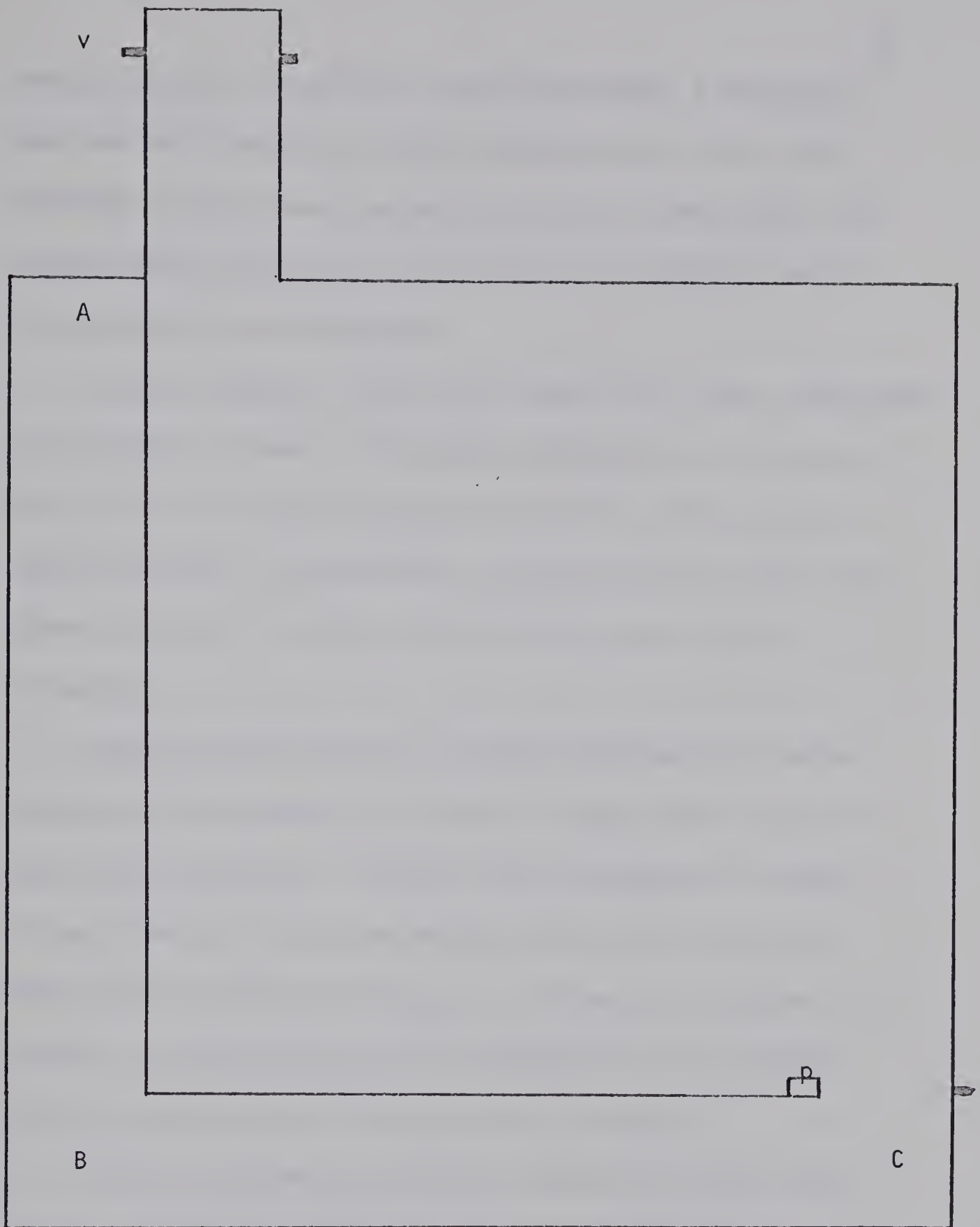


Figure 2. Floor Plan of the Maze Showing ABC--the Start Alley and p and v--the Photocells

handle the Ss. To provide latency measures, a photocell was mounted 1 in into the maze from the start box. The breaking of this beam started an electric timer which was stopped when the beam of a photocell 3 in from the end of the goal box was interrupted.

Watering Cages. These were a bank of 8 cages constructed of unpainted plywood. The inside dimensions of each cage were 6 in x 8 in x 18 in high and the floor was made of hardware cloth. On the front of each cage was a hole 3 in above the floor to admit the spout of a water bottle.

Procedure

Prior to the beginning of this experiment the lethal doses for this strain at the ages at which they were to be used were determined. Similar Wistar animals at 40 days of age (the age at the beginning of the first series of injections) exhibited an LD₅₀ of 2.02 mg/kg strychnine. At 70 days of age (the age at the beginning of the testing series of injections) the LD₅₀ was 2.67 mg/kg.

For the strychnine injections during the experiment itself, strychnine sulphate in its crystalline form was mixed with isotonic saline to give a concentration of 0.16 mg/cc of the anhydrous form. Injections of both strychnine and saline were given at a volume of 1 cc/kg of bodyweight. Therefore the animals in the drug groups received injections of 0.16 mg/kg body weight which was 8% and 6% of LD₅₀.

Rearing. The Ss were received at 21 days of age and this was considered day 1 of the experiment. At this time they were placed 4 to a cage to allow them to recover from travelling and to ensure that they were in good health. On day 8 one half of each litter was placed in one of the 2 group cages and the Ss from the other half were placed in single cages. For example, in the original part of the study, 4 animals from litter 1 and 4 animals from litter 2 were housed in one group cage, and 4 animals from litter 3 and 4 animals from litter 4 were housed in the second group cage. The remaining animals were placed under the restricted conditions. The Ss remained in these situations until day 21 of the experiment. On this day was begun a series of 12 daily injections: one half of the Ss received saline and the other half received strychnine. These injections were administered 8 hrs into the night part of the diurnal cycle which was the same for both groups of Ss. The animals were weighed daily to determine the volume of the injections to be administered. The overall average weight at this time was 149 gm. After this series of injections the Ss were maintained as before until day 39 when they were placed on a 23 hr water deprivation schedule. This continued until day 44 when pretraining was begun. Until day 39 all Ss had free access to both food and water.

Pretraining. This phase occupied 6 days of the procedure,

during which time the Ss experienced 6 practice problems (Fig. 1). All of pretraining was carried out in the night portion of the daily cycle and the only illumination was provided by a 60 watt red light bulb. With problem A the Ss were given 20 min free exploration in the maze with water available in the goal box. They received an additional 40 min of watering time in the watering cages after the exploration. With problem B the Ss had 4 discrete, massed trials, being allowed to drink for 10 sec upon reaching the goal box. With problem C they were given 7 massed trials and were allowed to drink for 5 sec upon attaining the goal box. On these latter two days the Ss were placed in the individual watering cages for 1 hr after being removed from the maze.

On the fourth day of pretraining Ss received 7 massed trials on problem D, were rested for 4 hrs and then were given the first trial of problem E. On the fifth day the procedure was repeated using problems E and F. On day 6 of pretraining Ss were given trials 2-8 of problem F and 4 hrs later problem 1 of the testing problems was used for 1 trial. Ten sec after completion of this single trial including the 5 sec goal box drinking time, the Ss were injected with the appropriate material.

Testing. The pretraining was arranged to shape the Ss to the procedure of the split running time which was used throughout testing (i.e., trials 2-8 of one problem, rest 4 hrs, trial

1 of the succeeding problem). By giving trial 1 on one day followed by an injection and trials 2-8 on the following day, the experimenter was able to evaluate the efficacy of post-trial injections upon retention of a single experience. That is, any difference between the groups that arose in the crucial trial 2 could be attributed to drug effects on learning.

From the beginning of water deprivation to the end of the experimental procedure Ss were never watered in their home cages. During the testing and the section of pretraining where maze experience was split, the animals were run approximately 19 1/2 hrs thirsty and the injections during testing were administered 6 to 10 hrs into the dark part of the cycle. At the beginning of testing the Ss weighed an average of 242 gm.

RESULTS

If there was an influence of strychnine upon consolidation effects, it should be reflected in the data of trial 2 which occurred approximately 20 hrs after trial 1 with its immediate post-trial injection, since this was the first measure taken after the time period when consolidation processes should have been occurring. For this reason an analysis of variance was performed on the error data of the second trial summed across problems.

The results are shown in Table 1 and the treatment means and standard deviations are given in Table 2. There is a significant effect of environment (enriched superior to restricted) and a significant interaction of environment by testing injections. Under the enriched condition, animals that received strychnine during testing made fewer errors than their controls, but under the restricted condition the animals that received strychnine during testing were inferior to those who received saline. A graphical representation of this interaction is shown in Figure 3 with the groups represented on the abscissa in the order of increasing drug in relation to the learning task.

To test for simple effects within the interaction Mann-Whitney U tests were carried out on the trial 2 error data and

TABLE 1
Analysis of Variance Summary Table for Trial
2 Errors Summed Across Problems

Source	SS	df	MS	F
Environment	1156.00	1	1156.00	48.43*
Early Injection	18.06	1	18.06	.76
Test Injection	95.06	1	95.06	3.98
Environment x Early Inj	16.00	1	16.00	.67
Envir x Test Inj	650.25	1	650.25	27.24*
Early Inj x Test Inj	22.56	1	22.56	.94
Envir x Early Inj x Test Inj	30.25	1	30.25	1.27
Error	1336.73	56	23.87	
Total	3324.91	63		

*p < .05

TABLE 2
Means and Standard Deviations of Trail 2 Errors Summed
Across Problems for Each of the Treatment Conditions

Environment: Enriched				Restricted			Total $\bar{X}$
Early Injection:	Strychnine	Saline		Strychnine	Saline		
Testing Injection							
Strychnine $\bar{X}$	29.87	28.62	29.25	43.23	43.75	43.44	36.34
S.D.	2.48	3.46		6.49	6.00		
Saline $\bar{X}$	32.50	32.50	32.50	37.00	33.56	35.28	33.89
S.D.	4.63	3.55		6.78	2.67		
Total $\bar{X}$	31.18	30.56	123.49	40.06	38.65	39.33	35.12
Total $\bar{X}$ Early Strychnine			35.62				
Total $\bar{X}$ Early Saline			34.61				

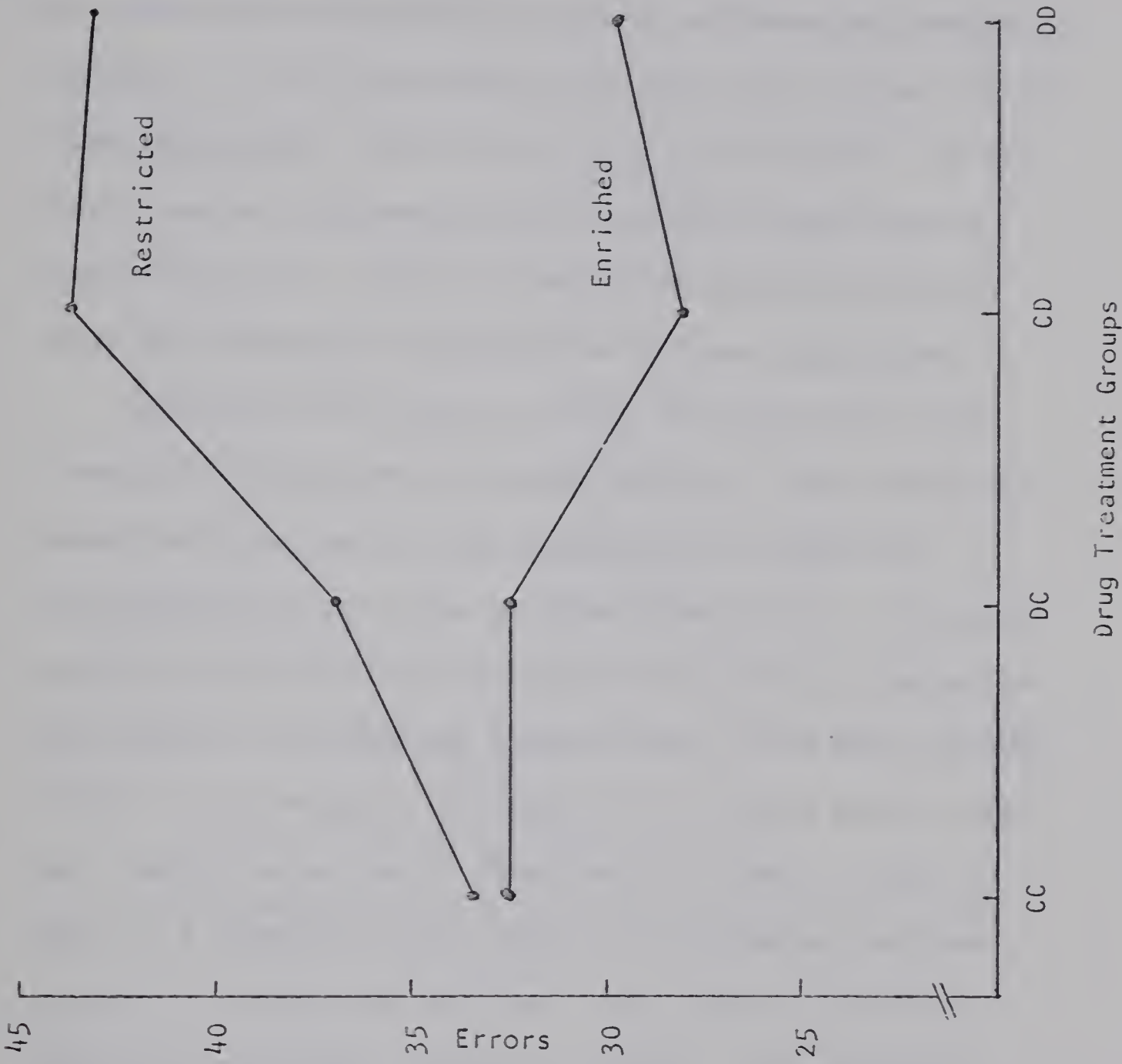


Figure 3. Graphical Representation of the Environment by Testing Injection Interaction for Trial 2 Data.

a tabulation of these results is given in Tables 3 and 4. Table 3 shows comparisons among drug treatments taken two at a time under the enriched condition and under the restricted condition. In the former case (enriched) there are two significant differences. CD is better than both DC and CC. In the latter case all differences are significant except the one between DD and CD. Table 4 shows the environmental effects where all differences except ECC vs. RCC are significant.

The sums of the errors on trials 3-8 were taken to be a measure of general maze learning ability. These trials were massed and there was no drug administered to affect the consolidation of the traces of these experiences. A factorial analysis of variance was performed on these data to determine the effects of experimental manipulations on the maze learning ability. This analysis is summarized in Table 5 and the means and standard deviations of these data are shown in Table 6. There is a significant main effect of environment (enriched superior to restricted) and also a main effect of testing injection (strychnine superior to saline). Mann-Whitney U tests were calculated for the interaction data as shown in Figure 4 for the total errors of trials 3-8 to compare the results with those found in the trial 2 data. A summary of the tests is given in Tables 7 and 8. In the enriched condition DD is significantly superior to both DC and CC, and also CD is significantly superior to CC. In the restricted condition there

TABLE 3

Results of the Mann-Whitney U Test for Differences Between
Groups on Errors in the Enriched and the Restricted Environments

Trial 2

Enriched	Restricted
DD < DC	DD > DC *
DD > CD	DD < CD
DD < CC	DD > CC *
DC > CD *	DC < CD *
DC = CC	DC > CC *
CD < CC *	CD > CC *

* $p < .05$

TABLE 4

Results of the Mann-Whitney U Test for
Differences between Environments on Errors

Trial 2

Enriched vs. Restricted
EDD < RDD *
EDC < RDC *
ECD < RCD *
ECC < RCC

* $p < .05$

TABLE 5
Analysis of Variance Summary Table for the Errors
on Trials 3-8 Summed Across Problems

Source	SS	df	MS	F
Environment	56882.25	1	56882.25	52.57*
Early Injection	27.56	1	27.56	.00
Testing Injection	4658.06	1	4658.06	4.31*
Envir x Early Inj	1040.06	1	1040.06	.96
Envir x Test Inj	976.56	1	976.56	.90
Early Inj x Test Inj	49.00	1	49.00	.00
Envir x Early Inj x Test Inj	6.26	1	6.26	.00
Error	60590.25	56	1081.97	
Total	124230.00	63		

*p < .05

TABLE 6
Means and Standard Deviations of Errors on Trials 3-8 Summed
Across Problems for Each of the Treatment Conditions

Environment: Enriched			Restricted				
Early Injection:	Strychnine	Saline	Strychnine	Saline			Total $\bar{X}$
Testing Injection							
Strychnine $\bar{X}$	68.12	76.38	72.25	144.25	135.23	139.68	105.97
S.D.	18.16	11.97		28.77	59.18		
Saline $\bar{X}$	91.88	102.38	97.13	151.12	146.75	148.94	123.03
S.D.	29.25	30.19		42.33	19.83		
Total $\bar{X}$	80.00	89.38	84.64	147.68	140.94	144.31	114.50
Total $\bar{X}$ Early Strychnine				113.86			
Total $\bar{X}$ Early Saline				115.16			

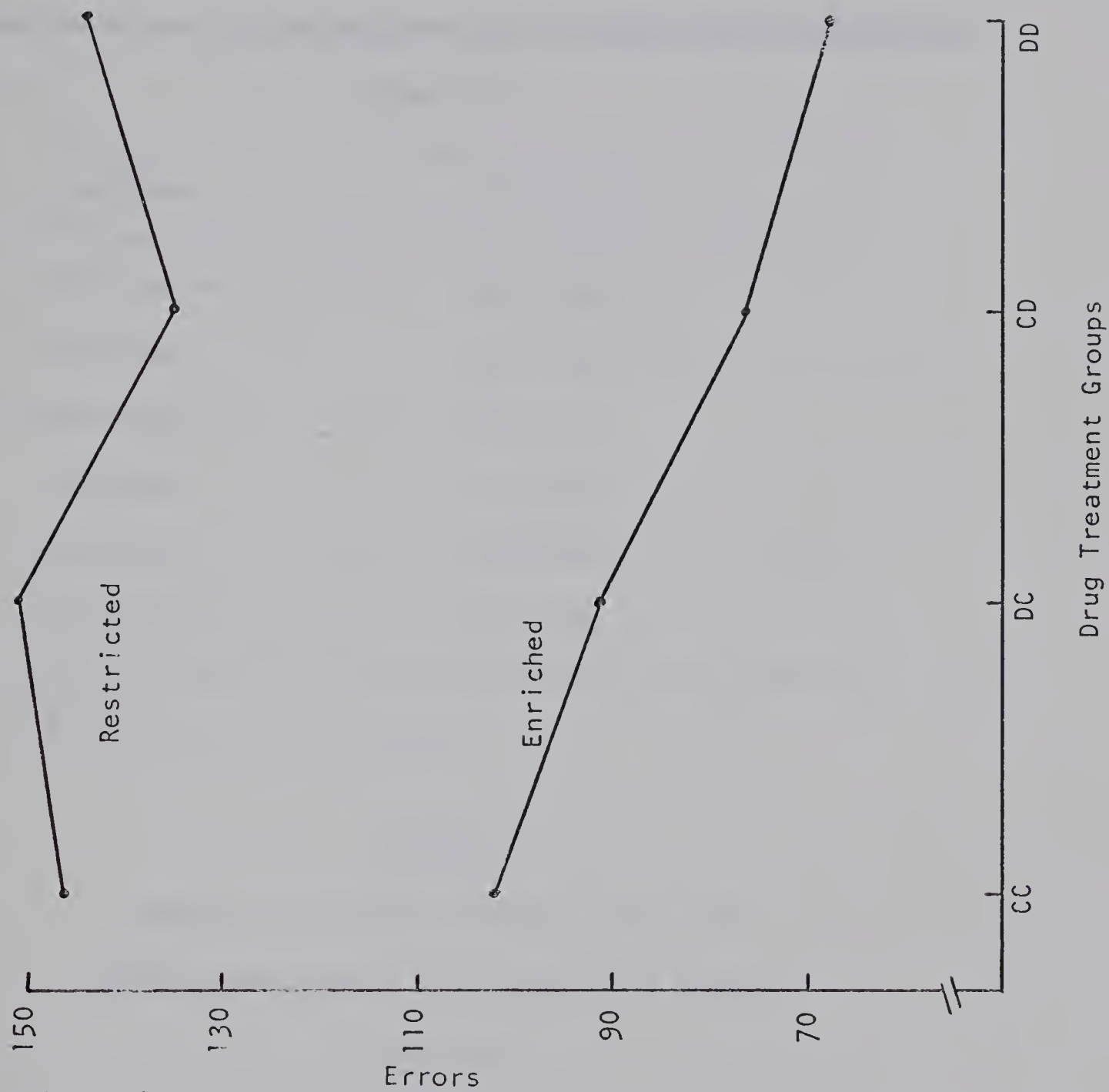


Figure 4. Graphical Representation of the Environment by Testing Injection Interaction for Trials 3-8 Data

TABLE 7

Results of the Mann-Whitney U Test for Differences Between
Groups on Errors in the Enriched and the Restricted Environments
Trials 3-8

Enriched	Restricted
DD < DC *	DD < DC
DD < CD	DD > CD
DD < CC *	DD < CC
DC > CD	DC > CD
DC < CC	DC > CC
CD < CC *	CD < CC

* $P < .05$

TABLE 8

Results of the Mann-Whitney U Test for
Differences Between Environments on Errors
Trials 3-8

Enriched vs. Restricted
EDD < RDD *
EDC < RDC *
ECD < RCD *
ECC < RCC *

* $p < .05$

are no significant differences. (Table 7). Table 8 shows that all the groups raised under the enriched condition performed significantly better than their corresponding groups reared in the restricted situation.

Figures 5 and 6 illustrate the effects of the various treatment conditions over trials. Figure 5 shows the pure environmental effect (ECC vs. RCC); Figure 6 the pure effects of the injection only at the time of testing for each environment (ECD vs. ECC, and RCD vs. RCC).

All groups weighed approximately the same at any given point throughout the experiment. The overall averages at the beginning of the experiment, on the first day of early injections, and on the first day of test injections were 73 gm, 149 gm and 242 gm respectively.

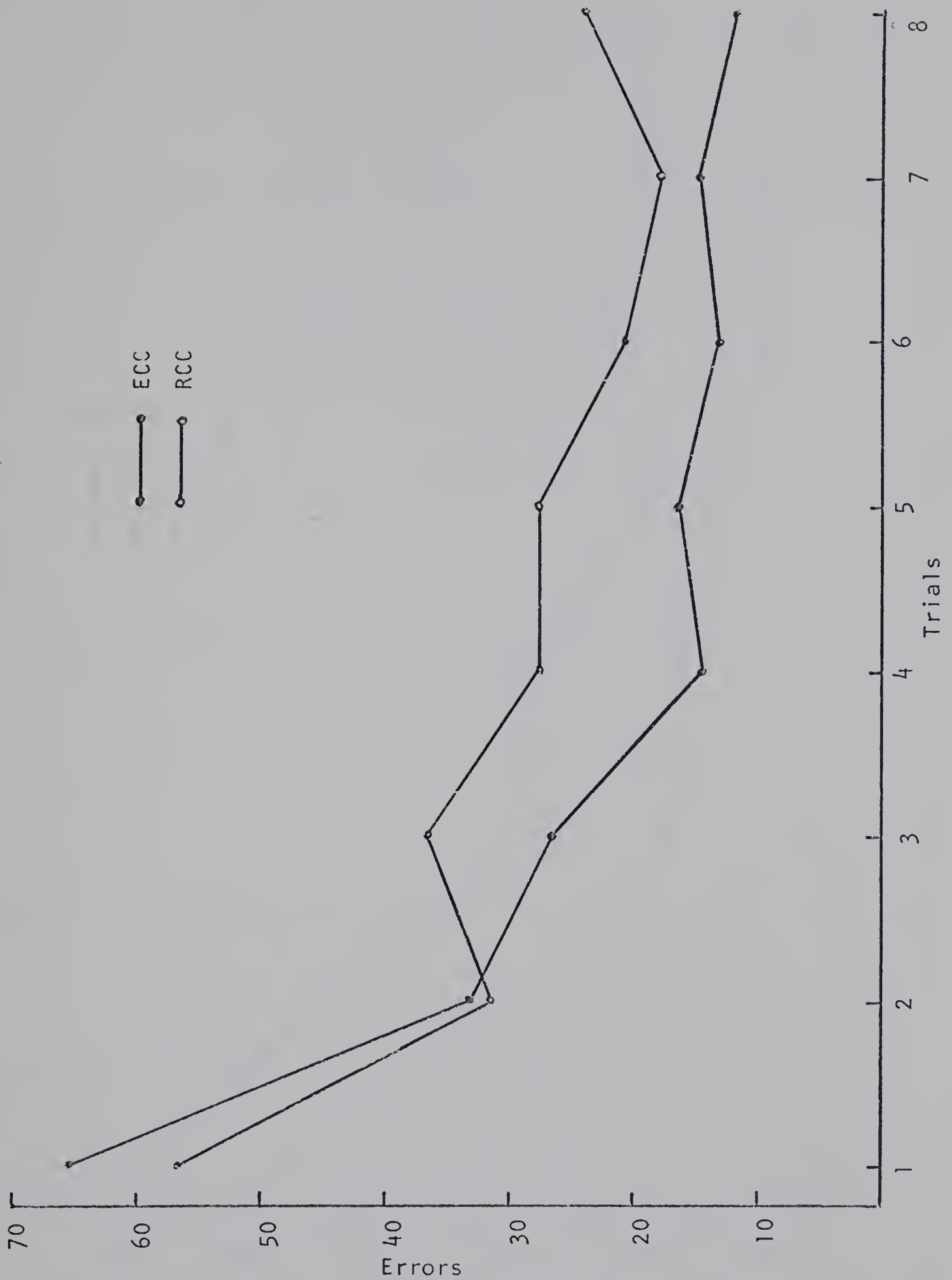


Figure 5. Mean Errors Over Trials for Groups ECC and RCC Showing the Pure Environmental Effect

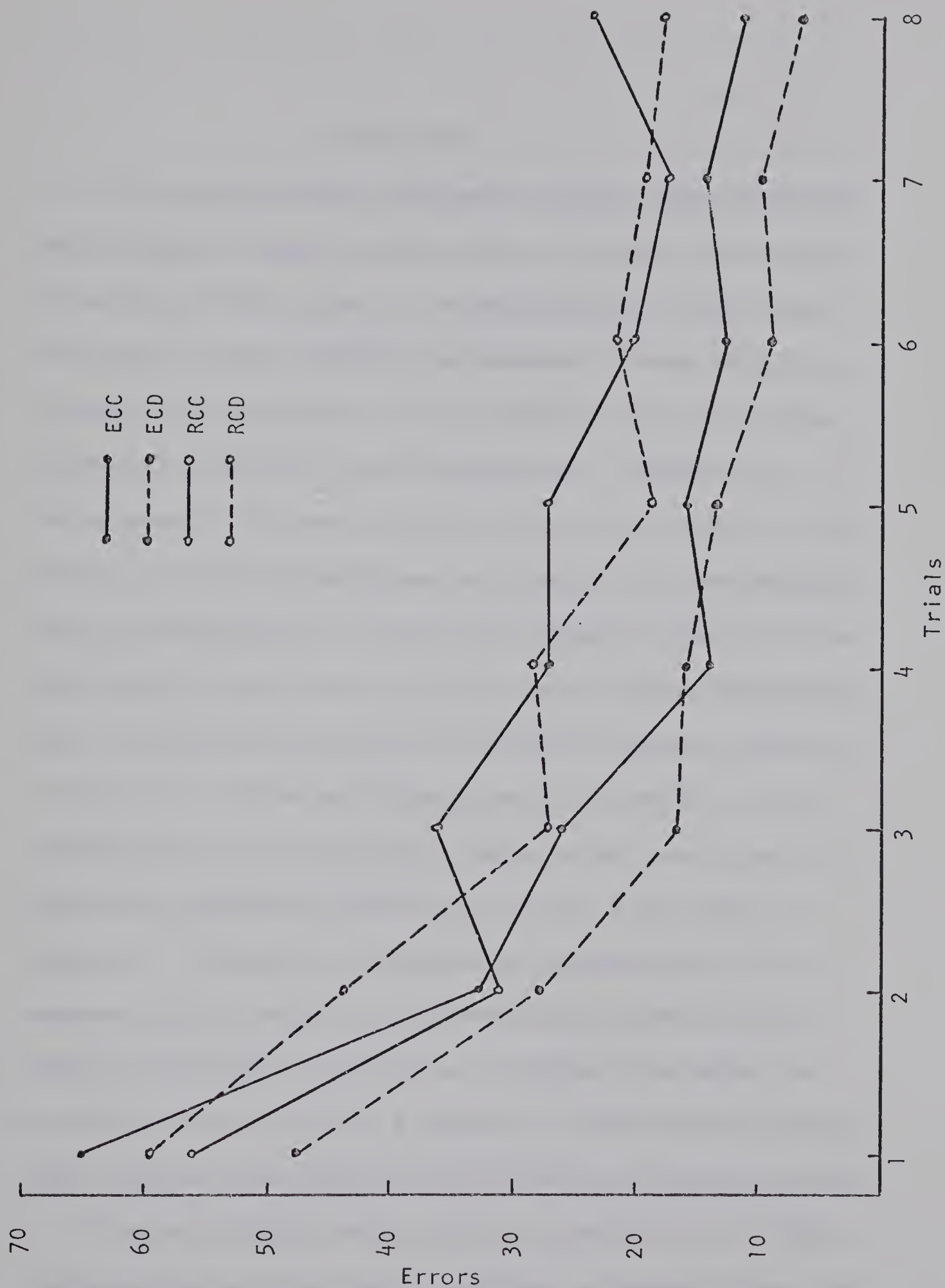


Figure 6. Mean Errors Over Trials for Groups ECD and ECC, and RCD and RCC Showing the Pure Effects of the Drug at the Time of Testing

DISCUSSION

The results of this experiment initially seem to confirm the findings of others of the effects of rearing environment on learning ability, that is, animals raised in an enriched environment exhibit superior performance to those raised in a restricted environment. This result is shown in the data of trial 2 as well as those of trials 3-8. However, it can be seen in the data of trial 2 that the comparison of the groups in this study which are most similar to those generally used in investigations of early environmental effects (ECC vs. RCC, Figure 3 and Table 4), show no significant differences at all. In the same comparison in trials 3-8, however, there is a significant difference between groups ECC and RCC. Upon examination of the experimental manipulations one finds a difference between the conditions of trial 2 and those of trials 3-8. There was an interval of approximately 20 hr between trials 1 and 2 but the intertrial interval between trials 3-8 was only 5 to 10 sec. Therefore, the effect was to make the data for trial 2 a measure of distributed practice while the data from trials 3-8 were measures of massed practice.

Thomson, McGaugh, Smith, Hudspeth, and Westbrook (1961) discussed the fact that under conditions of massed trials, the Tryon maze bright strain (S_1) of rats exhibit a consistent

superiority of learning a maze over the maze dull strain (S_3). However, this typical strain difference is not found if the practice is distributed. To account for these facts, Thomson et al. suggest that the difference between the strains is due to a differential rate of "... post trial consolidation of neural processes mediating maze behavior" (p. 69). That is, in the S_1 strain consolidation proceeds at a faster rate than in the S_3 strain. As a result distribution of practice eliminates strain differences by allowing for maximum consolidation in rats of both strains.

If one makes the assumption that the differential rearing conditions caused some change in the animals, making the enriched animals analogous to the S_1 strain and the restricted animals analogous to the S_3 strain (and behaviorally this is true as is evidenced by the differences found in maze learning), the same explanation can be used to interpret the differences found in the control groups' data of trial 2 and those of trials 3-8. That is, on trial 2 maximum consolidation had occurred in both the enriched and restricted Ss, but on trials 3-8 the faster rate of consolidation in the enriched Ss allowed them to exhibit a superiority in maze performance.

The fact that there is a significant main effect of environment in the trial 2 data can be explained by considering the strychnine groups. The locus of the difference in the performance of the two rearing conditions lies primarily in the

poorer performance of the restricted animals who had received strychnine at any time in their history and to some extent the improved performance of the enriched groups that received strychnine at the time of testing. Table 3 shows that all of the trial 2 comparisons between the restricted control group and any restricted strychnine group were significantly different with the group that had received strychnine making more errors. Furthermore, receiving the drug only at the time of testing or both at the time of testing and earlier in life was more potent in producing the deficit than being injected only earlier in life since both RCD and RDD made significantly more errors than RDC. This indicates that strychnine injections tend to impair performance of restricted animals on distributed practice. Also, the injection of the drug has long-lasting effects on this behavior since RDC made significantly more errors than RCC. It is further shown for the trial 2 data that in the enriched environment, strychnine shows a facilitory effect with ECD significantly superior to EDC and ECC and although group EDD did not show a difference at the .05 probability level, the probability of EDD being superior to EDC and ECC was .08.

To explain the differential effects of the drug on the Ss that are reared differently one must again consider the consolidation process. In the enriched Ss this process proceeds at its maximum rate and the increase in neural activity due to the action of the drug has no effect in improving consolidation.

However, in the animals raised in the restricted condition, in spite of the fact that their process of consolidation has room for improvement, as it is in the control group with distributed practice, the introduction of strychnine likely raises the level of neural activation to a point that causes a disruption of consolidation. This may be due to the fact that the restricted animals were kept for a relatively long period in a state of minimal stimulation and were thereafter unable to utilize greatly increased neural activity. On the other hand, the Ss raised in the enriched environment had been surrounded daily by much activity with its resulting stimulation, and so were more capable of handling any increase in neural activity resulting from the drug. In fact, the combination of the drug and the closed environment of the watering cages where the drug had its major effect may have produced a level of neural activity comparable to what, for the enriched animals, was normal.

In the data of trials 3-8, that is, the data reflecting massed practice, we see by Figure 4 and Table 5 that there is a large main effect of environment. Table 8 shows further that all enriched groups made significantly fewer errors than their respective restricted groups. However, with respect to a drug effect, we find that in this case there are no differences among the restricted groups (Table 7), and that among the enriched groups the comparisons of EDD with ECC and EDC

and ECD with ECC yield significant differences, that is a superiority of drug over control in all cases.

The environmental main effect appears to be due to the fact that the enriched animals are capable of more rapid consolidation, which is necessary in the massed practice situation, than the restricted animals are.

The lack of differences among the restricted groups should be expected in these data since there should have been no influence of the drug on trials 3-8; therefore, all the restricted groups should have performed equally poorly due to their slow consolidation processes. In the restricted groups on distributed practice, strychnine leads to poorer performance while the control group can show the maximum level of performance possible for the restricted groups. However, on the massed trials, the control subjects are brought down to the maximally poor performance of restricted strychnine groups. By the same token (i.e., no drug influence on trials 3-8) one should not expect to find any consolidation differences due to the drug among the enriched groups either. They should all have performed equally well. However, as is shown in Figure 4, there is a definite trend for experience with strychnine to result in better performance and indeed, EDD performed significantly better than both ECC and EDC and ECD was superior to ECC. A possible explanation for this is that the combination of the Ss experience of the enriched environment combined with

possible long lasting effects of the drug enables these animals to make better use of their experience probably through more rapid consolidation. That is, the brain of an animal that receives strychnine in an enriched environmental situation becomes more capable of rapidly consolidating neural traces. This may merely be a function of usage of neural pathways. The same stimulation at learning is of no benefit to the restricted Ss since it overloads the brain which has a minimal number of pathways developed.

It seems that strychnine and rearing environment interact in a complex manner. The immediate effect of the drug upon the consolidation of a single experience of distributed practice is to disrupt it in the case of animal raised in a restricted environment and to increase consolidation in those raised in an enriched environment. This may be due to the fact that in the enriched condition strychnine has its effect on the rate of consolidation while in the restricted condition the increase in stimulus input gives rise to too much cortical "noise" for the learning input to be utilized. That is, a different signal-to-noise ratio arises in the two groups. The drug in the enriched condition gives rise to increased signal, while in the restricted condition the drug results in increased noise. Similarly, in the massed practice conditions, all restricted groups perform equally poorly since even the non-drug group experiences increased noise due to the close spacing of the

trials. Such massed experience for the enriched Ss is better handled by the strychnine groups than by the non-drug groups via the same signal-to-noise ratio mechanism.

To lend more weight to these conclusions it would be necessary to study further the parameters of degree of deprivation and enrichment. It would be particularly valuable to determine at what period of sensory restriction during rearing the drug becomes disruptive. Also it seems necessary to determine the dose range of the observed effects. It is plausible that some other dose might have caused an enhancement of maze behavior in the restricted animals. Another parameter that might have been studied is the degree of massing of practice to determine what degree of distribution is required for adequate consolidation to take place in the restricted animals.

B I B L I O G R A P H Y

References

- Anderson, P., Eccles, J. C., Løyning, Y., & Voorhoeve, P. E. Strychnine-resistant central inhibition. Nature, 1963, 199, 843-845.
- Benevento, L. A. & Kandel, G. L. Influence of strichnine on classically conditioned reflexes in the cat. J. comp. physiol. Psychol., 1967, 63, 117-120.
- Bingham, W. E. & Griffiths, W. J., Jr. The effect of different environments during infancy on adult behavior in the rat. J. comp. physiol. Psychol., 1952, 45, 307-312.
- Bovet, D., McGaugh, J. L., & Oliverio, A. Effects of post trial administration of drugs on avoidance learning. Life Sciences, 1966, 5, 1309-1315.
- Bradley, K., Easton, D. & Eccles, J. An investigation of primary or direct inhibition. J. Physiol., Lond., 1953, 122, 474-488.
- Calhoun, W. H. Effect of level of external stimulation on rate of learning and interaction of this effect with strychnine treatment in mice. Psychol. Rep., 1966, 18, 715-722.
- Carlson, K. Note on strychnine sulphate, general activity and facilitation of learning. Psychol. Rep., 1964, 15, 145-146.
- Cooper, R. M. & Krass, M. Strychnine: duration of the effects on maze learning. Psychopharmacology, 1963, 4, 472-475.
- Curtis, D. R. Pharmacological investigations upon inhibition of spinal motoneurones. J. Physiol., Lond., 1959, 145, 175-192.
- Curtis, D. R. The depression of spinal inhibition by electrophoretically administered strychnine. Int. J. Neuropharmacol., 1962, 1, 239-250.
- Desmedt, J. E. & Monaco, P. Archs. Int. Pharmacodyn. Thé. 1960, 129, 224-248.

- Dews, P. B. Measurement of the influence of drugs on voluntary activity in mice. Br. J. Pharmac. Chemother. 1953, 8, 46-48.
- Diamond, M. C., Krech, D., & Rosenzweig, M. R. The effects of enriched environment on the histology of the rat cerebral cortex. J. comp. Neurol., 1964, 123, 111-119.
- Doolittle, J. H. & Thomson, C. W. Retroactive effects of topical applications of potassium chloride, pentylene-tetrazol, and strychnine on the acquisition of a maze habit in rats. Psychon. Sci., 1966, 5, 265-266.
- Eccles, J. C., Fatt, P., & Koketsu, K. Colinerergie and inhibitory synapses in a pathway from motor-axon collaterals to motoneurones. J. Physiol., Lond., 1954, 126, 524-562.
- Forgays, D. G., & Forgays, J. W. The nature of the effect of free-environmental experience in the rat. J. comp. physiol. Psychol., 1952, 45, 322-328.
- Gibby, R. G., Sr., Gibby, R. G., Jr., Kish, G., & Theologas, G. Enhancement of avoidance learning by strychnine sulphate. Psychol. Rep., 1965, 17, 123-126.
- Greenough, W. T. & McGaugh, J. L. The effect of strychnine sulphate on learning as a function of time of administration. Psychopharmacology, 1965, 8, 290-294.
- Goodman, L. S. & Gilman, A. The pharmacological basis of therapeutics. (3rd ed.) New York: MacMillan, 1965.
- Hebb, D. O. The organization of behavior. New York: John Wiley & Sons, 1949.
- Heinbecker, P. & Barley, S. H. Manner of strychnine action on nervous system. Am. J. Physiol., 1939, 172-187.
- Hudspeth, W. Strychnine: Its facilitating effect on the solution of a simple oddity problem by a rat. Science, 1964, 145, 1331-1333.
- Hull, C. L. Essentials of behavior. New Haven: Yale University Press, 1951.
- Hynovitch, B. The effects of experimental variations on problem solving in the rat. J. comp. physiol. Psychol., 1952, 45, 313-321.

- Keleman, K. & Bovet, D. Effect of drugs upon the defensive behavior of rats. Acta physiol. scand., 1961, 19, 143-154.
- Krech, D., Rosenzweig, M. R. & Bennett, E. L. Effects of environmental complexity and training on brain chemistry. J. comp. physiol. Psychol., 1960, 53, 509-519.
- Krech, D., Rosenzweig, M. R. & Bennett, E. L. Relations between brain chemistry and problem solving among rats raised in enriched and impoverished environments. J. comp. physiol. Psychol., 1962, 55, 801-807.
- Krivanek, J. & Hunt, E. The effects of posttrial injections of pentylenetetrazole, strychnine and mephenesin on discrimination learning. Psychopharmacology, 1967, 10, 189-195.
- Lashley, K. S. The effect of strychnine and caffeine upon rate of learning. Psychology, 1917, 1, 141-170.
- Louttit, R. T. Central nervous system stimulants and maze learning in rats. Psychol. Rec., 1965, 18, 97-101.
- McGaugh, J. L. Facilitative and disruptive effects of strychnine sulphate on maze learning. Psychol. Rep., 1961, 8, 99-104.
- McGaugh, J. L. Drug facilitation of memory learning. (unpublished) Sixth Annual Meeting of the American College of Neuropsychopharmacology, San Juan, Puerto Rico, 1967.
- McGaugh, J. L. & Petrinovich, L. The effect of strychnine sulphate on maze-learning. Am. J. Psychol., 1959, 72, 99-102.
- McGaugh, J. L. & Petrinovich, L. Comments concerning the basis of learning enhancement with central nervous system stimulants. Psychol. Rep., 1963, 12, 211-214.
- McGaugh, J. L. & Thomson, C. S. Facilitation of simultaneous discrimination learning with strychnine sulphate. Psychopharmacology, 1962, 3, 166-172.
- McGaugh, J. L., Thomson, C. S., Westbrook, W. H., & Hudspeth, W. J. A further study of learning facilitation with strychnine sulphate. Psychopharmacology, 1962, 3, 352-360.

- Otis, L. S. & Pryor, G. T. Lack of effect of strychnine on learning. Paper presented at the Western Psychological Association, 1968.
- Petrinovich, L. Facilitation of successive discrimination learning by strychnine sulphate. Psychopharmacology, 1963, 4, 103-113.
- Petrinovich, L. Drug facilitation of learning: Strain differences. Psychopharmacology, 1967, 10, 375-378.
- Petrinovich, L., Bradford, D., & McGaugh, J. L. Drug facilitation of memory in rats. Psychon. Sci., 1965, 2, 191-192.
- Prien, R. F., Wayner, M. J., & Kahan, S. Lack of facilitation in maze-learning by picrotoxin and strychnine sulphate. Am. J. Physiol., 1963, 204, 488-492.
- Purpura, D. P. & Grundfest, H. Physiological and pharmacological consequences of different synaptic organizations in cerebral and cerebellar cortex of the cat. J. Neurophysiol., 1957, 20, 494-522.
- Rabinovitch, M. S. & Rosvold, H. E. A closed-field intelligence test for rats. Can. J. Psychol., 1951, 5, 122-128.
- Rosenzweig, M. R. Environmental complexity, cerebral change, and behavior. Am. Psychol., 1966, 21, 321-332.
- Rozenzweig, M. R., Krech, D., Bennett, E. L., & Diamond, M. C. Effects of environmental complexity and training on brain chemistry and anatomy: A replication and extension. J. comp. physiol. Psychol., 1962, 55, 429-437.
- Ross, R. B. Effects of strychnine sulphate on maze learning in rats. Nature, 1964, 201, 109-110.
- Schaeffer, B. H. Strychnine and maze behavior: Limited effects of varied concentrations and injection times. J. comp. physiol. Psychol., 1968, 66, 188-192.

- Schiller, P. H. & Chorover, S. L. Short-term amnestic effects of electroconvulsive shock in a one-trial maze learning paradigm. Neuropsychologica, 1967, 5, 155-163.
- Thiessen, D., Schlesinger, K., & Calhoun, W. Better learning: Neural enhancement or reduced interference. Psychol. Rep., 1962, 9, 493-496.
- Thomson, C. W., McGaugh, J. L., Smith, C. E., Hudspeth, W. J., & Westbrook, W. H. Strain differences in the retroactive effects of electroconvulsive shock on maze learning. Can. J. Psychol., 1961, 15, 69-74.
- Westbrook, W. & McGaugh, J. L. Drug facilitation of latent learning. Psychopharmacology, 1964, 5, 440-446.
- Woods, P. J., Fiske, A. S. & Ruckelshaus, S. I. The effects of drives conflicting with exploration on the problem solving behavior of rats raised in free and restricted environments. J. comp. physiol. Psychol., 1961, 54, 167-169.

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